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EXAMINER
BLAKELY III, NELSON CLARENCE

ART UNIT	PAPER NUMBER
1614	

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08/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,892	GEBICKI ET AL.	
	Examiner	Art Unit	
	NELSON C. BLAKELY III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-64,70-72,74-84 and 86-89* is/are pending in the application.

4a) Of the above claim(s) *59-62,64 and 81-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57,58,63,70-72,74-80 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 May 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/21/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 57-64, 70-72, 74-84 and 86-89 of the instant application are pending. Claims 59-62, 64 and 81-84 are withdrawn pursuant to Applicant's Amendment, filed 05/21/2009. Accordingly, instant claims 57, 58, 63, 70-72, 74-80 and 86-89 are presented for examination on their merits.

Applicant's Arguments, filed 05/21/2009, have been fully considered. Rejections/objections not reiterated from previous Office Actions are hereby ***withdrawn***. The following rejections/objections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Information Disclosure Statement

The Information Disclosure Statement, filed 05/21/2009, is acknowledged and considered.

Applicant's Amendment

Applicant's Amendment, filed 05/21/2009, wherein the specification and claims 57, 77 and 81 are amended, claims 59-62, 64 and 81-84 are withdrawn, and claims 1-56, 65-69, 73 and 85 are canceled, is acknowledged.

Response to Arguments

The rejection of claims 57, 58, 63, 70-72, 74-80, 88 and 89, previously rejected under 35 U.S.C. 112, first paragraph, is hereby **withdrawn** pursuant to Applicant's Amendment filed 05/21/2009.

The rejections of claim 77, previously rejected under 35 U.S.C. 112, first and second paragraphs, are hereby **withdrawn** pursuant to Applicant's Amendment filed 05/21/2009.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57, 58, 63, 74-76, 78 and 86-89 were rejected under 35 U.S.C. 103(a) as being unpatentable over Carlson *et al*. (Atherosclerosis, Vol. 16, pages 359-368; 1972; Cited by Applicant), in view of Gębicki *et al*. (Polish Journal of Pharmacology, Vol. 55, pages 109-112; 2003; Cited by Applicant), as evidenced by Oettgen *et al*. (Cancer Research, Vol. 20, pages 1597-1601; 1960).

With regard to instant claims 57, 58, 63, 74-76 and 86-89, Carlson *et al*. disclose, in the Summary, a case of massive hypertriglyceridemia with fasting triglycerides, wherein large amounts of chylomicra were present in fasting plasma, and the amounts of low-density (LDL) and high-density lipoproteins (HDL) were very low (instant claims 63 and 87-89). In the instant excerpt, Carlson *et al*. further disclose wherein nicotinic acid or nicotinamide was administered to reduce plasma triglyceride levels to about 2-3 mmoles/L and raised the reduced levels of low- and high-density lipoproteins.

Carlson *et al*. fail to disclose specifically wherein formula I comprises a methyl group at the 1-position, or wherein R is CH_3 or $N(H)CH_2OH$. However, Gębicki *et al*. disclose, in the Introduction, the homologue, or analog, 1-methylnicotinamide (MNA+) as one of the two major primary metabolites of nicotinamide (NA). Gębicki *et al*. further disclose, in the instant excerpt, wherein it is well known that NA possesses remarkable anti-inflammatory properties, and that MNA+, similar to NA, is chemically stable, non-toxic and well tolerated. Furthermore, in the Results and Discussion, first paragraph, Gębicki *et al*. disclose that MNA+ can be used to treat a wide variety of skin diseases,

for example, and that the use of the compound also provides certain advantages over the use of NA, in particular, an increased efficacy at a specified dose and/or a reduction in undesirable side effects. In the instant excerpt, Gębicki *et al*. further disclose that when used topically, MNA+-containing gel has been shown to produce at least a similar therapeutic effect at concentrations approximately 100 times lower than the corresponding NA treatment with no appreciable side effects. Additionally, Oettgen *et al*. disclose, in Charts 1 and 2 and Table 1, wherein N-(hydroxymethyl)nicotinamide, wherein instantly claimed R is $N(H)CH_2OH$, and 3-acetylpyridine, wherein instantly claimed R is CH_3, were equally as potent as nicotinamide, wherein instantly claimed R is NH_2, and nicotinic acid (See page 1599, column 2, first full paragraph).

Therefore, a skilled artisan would have envisaged the instantly claimed formula I, wherein R is NH_2, CH_3 or $N(H)CH_2OH$, in the treatment of hypertriglyceridemia, as disclosed by Carlson *et al*., in view of Gębicki *et al*., as evidenced by Oettgen *et al*. One of ordinary skill in the art would have been motivated to combine the teachings of the aforementioned references when seeking a method for treating hypertriglyceridemia, wherein a compound of formula I, with an increased efficacy at a specified dose and/or a reduction in undesirable side effects, is administered. It would have been obvious to one of ordinary skill in the art, at the time of the invention, because the combined teachings of the prior art are fairly suggestive of the claimed invention.

Accordingly, the instant invention, as claimed in claims 57, 58, 63, 74-76, 78 and 86-89, is *prima facie* obvious over the combination of the aforementioned teachings.

Applicant's Arguments

Applicant alleges the Examiner has made the assumption that from the mere fact that 1-methylnicotinamide is a metabolite of nicotinamide, it follows that any known therapeutic action of nicotinamide should be exerted via its known metabolite. In other words, apparently, Applicant alleges, the assumption has been made by the Examiner that in the treatment of hypertriglyceridemia, nicotinamide (and nicotinic acid) is a "prodrug" of 1-methylnicotinamide.

Further, Applicant alleges Gębicki *et al*. disclose that 1-methylnicotinamide (MNA) has use in the treatment of skin diseases by topical administration to the skin. There is no motivation to extend this teaching to the use of MNA in lipid profile disorders. Applicant alleges that such motivation cannot be found in Gębicki *et al*. – it could be found only in the present specification - such approach, however, is only with having the benefit of Applicant's specification, and therefore, is an unallowable hindsight.

Applicant argues that Gębicki *et al*., in accordance with the then general knowledge, disclose that 1-methylnicotinamide is one of two major primary metabolites of nicotinamide. However, there is nothing in Gębicki *et al*. to suggest that nicotinamide is inactive as such, and would NOT exert its function disclosed in Carlson *et al*. without earlier conversion to 1-methylnicotinamide. Such assumption, if at all, could only be made in contradiction with the then existing general knowledge on the role and active forms of nicotinamide.

Additionally, Applicant alleges that any similarity of the structures between nicotinamide and MNA, and other quaternary pyridinium salts of formula I from the

present application, is only "superficial" and does not imply similarity of biological actions. The addition of a methyl group to the nitrogen atom of the pyridine ring of nicotinamide results in a molecule that belongs to a different class of compounds, namely quaternary pyridinium salts, that, contrary to nicotinamide, have an ionic character and behave in a different manner in biological systems.

Applicant alleges, keeping in mind that it is general knowledge that the role of nicotinamide in living organisms and the mechanism of this role, the fact that MNA is the known metabolite of nicotinamide does not imply that nicotinamide exerts its function via MNA. Applicant further alleges, by evidence of the NPL reference (Harper's Biochemistry, Twenty-second edition., pages 549-551; 1990) that, in order to exert its functions in a living body, nicotinamide must be first converted to NAD+ and NADP+. Further, Applicant alleges that 1-methylnicotinamide is shown not to be involved in a manner in transformations leading to biosynthesis of NAD and NADP, and for these reasons, this metabolite of nicotinamide, for many years, has been considered inactive, wherein the only known function thereof was as the marker of the level of nicotinamide in a body.

Applicant alleges that in the last two paragraphs on page 366 and 367, Carlson *et al*. disclose that nicotinic acid should be linked with NAD/NADH system:

> "further studies should be directed towards NAD(H) dependent esterifying processes in this and other cases of hypertriglyceridemia."

Additionally, Applicant alleges there is nothing in Carlson *et al*. that could lead to any metabolite of nicotinamide other than nicotinic acid. On the contrary, because

Carlson *et al*. teaches that the same action is exerted by nicotinamide AND its metabolite nicotinic acid, one skilled in the art would link such action with the NAD system, as both these compounds are involved in this metabolic pathway. A person skilled in the art would not expect that 1-methylnicotinamide, which is not involved in the pathway leading to active forms of nicotinamide, and which is considered to be "a dead end" of nicotinamide metabolism, would have antihypertriglyceridemic action. Antihypertriglyceridemic activity of 1-methylnicotinamide and its two analogues covered by formula I could not be expected in view of Carlson *et al*. and Gębicki *et al*.

Applicant argues that there is no mention of any activity of 3-acetylpyridine and N-hydroxymethylnicotinamide, or their 1-methylated salts, with respect to lipid profile, including antihypertriglyceridemic activity.

Examiner's Response

Applicant's Arguments, filed 05/21/2009, have been fully considered but they are not persuasive.

The Examiner respectfully disagrees with Applicant's summation of the Examiner's "assumption". Gębicki *et al*. clearly disclose, in the *Introduction*, last paragraph, wherein 1-methylnicotinamide (MNA+), one of the two major primary metabolites of nicotinamide (NA), may be used to treat a wide variety of diseases and disorders, and the use of this compound provides certain advantages over the use of NA. Further, Gębicki *et al*. provide, in the *Results and Discussion* section, first paragraph, an example of treatment of skin diseases, wherein MNA+ has certain advantages over NA, in particular, with regard to an increased efficacy at a specified

dose and/or a reduction in undesirable side effects. Further, with regard to the example of treatment of skin diseases, e.g., acne, Gębicki *et al*. disclose, in the instant excerpt, wherein MNA+ has been shown to produce at least a similar therapeutic effect at concentrations approximately 100 times lower than the corresponding NA treatment, and with no appreciable side effects. Therefore, a skilled artisan, at the time of the invention, would have envisaged a method of treatment administering nicotinamide would have yielded substantially similar, if not better, results upon the administration of 1-methylnicotinamide, a primary metabolite thereof.

The Examiner acquiesces with Applicant in that Gębicki *et al*. fail to disclose 1-methylnicotinamide in the treatment of lipid profile disorder, e.g., hypertriglyceridemia. However, Gębicki *et al*. does disclose wherein 1-methylnicotinamide may be used to treat a wide variety of diseases and disorders, and the use of this compound provides certain advantages over the use of nicotinamide. Therefore, without the use of "unallowable hindsight" reasoning, one of ordinary skill in the art, at the time of the invention, would have construed the advantageous use of 1-methylnicotinamide in the treatment of hypertriglyceridemia, as disclosed by Carlson *et al*., in view of Gębicki *et al*.

Carlson *et al*. disclose, in the Summary, the administration of nicotinamide given in doses of 3 g or more daily to reduce plasma triglyceride levels and to raise the reduced levels of low and high-density lipoproteins. In this case, the allegation, as provided by Applicant, that nicotinamide “would not exert its function disclosed in Carlson *et al*. without earlier conversion to 1-methylnicotinamide” is irrelevant. “The use of patents as references is not limited to what the patentees describe as their own

inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)) and MPEP § 2123. Likely so, Carlson *et al*. disclose the administration of nicotinamide to treat hypertriglyceridemia. Whether or not nicotinamide has to convert to 1-methylnicotinamide in order to exert its function has no basis with regard to the instant reference.

The Examiner further acquiesces with Applicant in that any similarity of the structures between nicotinamide and 1-methylnicotinamide, and other quaternary pyridinium salts of Formula I, is "superficial" and **may** not imply similarity of biological actions. However, as evidenced by Patani *et al*. (Chem. Rev., Vol. 96, No. 8, pages 3147-3176; 1996), bioisosterism represents one approach used by the medicinal chemist for the rational modification of lead compounds into safer and more clinically effective agents, wherein the concept of bioisosterism is often considered to be qualitative and intuitive (See *Introduction*, page 3147, first paragraph). Further, on page 3153, paragraph bridging columns 1 and 2, and Table 12, Patani *et al*. disclose Compounds 20b (-CH_3) and 20e (H, or unsubstituted), exhibiting inhibitory activity of thymidylate synthase, for example, wherein the IC_{50} was 0.178 μM and 1.08 μM, respectively. In the instant excerpt, Patani *et al*. further disclose that within this series (Table 12), it was observed that hydrogen bond donors, e.g., Compound 20b, were more potent than the unsubstituted parent compound, e.g., Compound 20e. Therefore, one of ordinary skill in the art, at the time of the invention, would have been motivated,

through the art of bioisosterism, to chemically modify lead compounds into a more clinically effective agent.

The Examiner acknowledges Applicant's arguments, evidenced by the Harper's Biochemistry reference. It was not the intention of the Examiner to conclude that nicotinamide "exerts its function via MNA". The Examiner regrets any inadvertent misinterpretation. As stated *supra*, Carlson *et al*. disclose, in the Summary, the administration of nicotinamide to reduce plasma triglyceride levels and to raise the reduced levels of low and high-density lipoproteins. In this case, the allegation, as provided by Applicant, that nicotinamide would not exert its function disclosed in Carlson *et al*. without first being converted to NAD+ and NADP+ is irrelevant. See *In re Heck*, *In re Lemelson* and MPEP § 2123 discussion *supra*. Likely so, Carlson *et al*. disclose the administration of nicotinamide to treat hypertriglyceridemia. Whether or not nicotinamide has to convert to NAD+ and/or NADP+ in order to exert its function has no basis with regard to instant reference.

The Examiner brings to the attention of the Applicant that the quoted reference is with regard to the inhibition of free fatty acid (FFA) release from adipose tissue induced by nicotinic acid. Further, in the last paragraph, on page 367, Carlson *et al*. disclose that if the defect in removal of plasma triglycerides is related to a reduced esterification in tissues, e.g., adipose tissue, of fatty acids released from circulating triglycerides, and if the therapeutic responses are related to the levels in such tissues of NAD(H), further studies should be directed towards NAD(H) dependent esterifying processes in this and other cases of hypertriglyceridemia. The Examiner acquiesces with Applicant in that

Carlson *et al*. disclose only the use of nicotinic acid and nicotinamide in hypertriglyceridemia. Further, as mentioned *supra*, the Examiner acquiesces with Applicant in that Gębicki *et al*. fail to disclose 1-methylnicotinamide in the treatment of lipid profile disorder, e.g., hypertriglyceridemia. However, Gębicki *et al*. do disclose wherein 1-methylnicotinamide may be used to treat a wide variety of diseases and disorders, and the use of this compound provides certain advantages over the use of nicotinamide, such as increased efficacy and reduction in undesirable side effects. Therefore, one of ordinary skill in the art, at the time of the invention, would have construed the advantageous use of 1-methylnicotinamide in the treatment of hypertriglyceridemia, as disclosed by Carlson *et al*., in view of Gębicki *et al*.

The Examiner acquiesces with Applicant in that there is no mention in Oettgen *et al*. of any activity of 3-acetylpyridine and N-hydroxymethylnicotinamide, or their 1-methylated salts, with respect to lipid profile, including antihypertriglyceridemic activity. However, as mentioned *supra*, Oettgen *et al*. disclose, in Chart 1 and 2, pages 1598 and 1599, and page 1599, first full paragraph, wherein N-hydroxymethyl-nicotinamide and 3-acetylpyridine were equally as potent as nicotinamide with regard to their antileukemic activity. Therefore, when considering the teachings of Carlson *et al*., in view of Gębicki *et al*. and Oettgen *et al*., a skilled artisan, at the time of the invention, would have envisaged three substantially similar compounds, in structure and biological activity, as disclosed by Oettgen *et al*. and Gębicki *et al*., in the treatment of hypertriglyceridemia with a reasonable expectation of success, as disclosed by Carlson *et al*.

The rejection of claims 57, 58, 63, 74-76, 78 and 86-89 is **maintained**.

Claims 70-72, 77, 79 and 80 were rejected under 35 U.S.C. 103(a) as being unpatentable over Carlson *et al*. (Atherosclerosis, Vol. 16, pages 359-368; 1972), in view of Gębicki *et al*. (Polish Journal of Pharmacology, Vol. 55, pages 109-112; 2003; Cited by Applicant), as evidenced by Oettgen *et al*. (Cancer Research, Vol. 20, pages 1597-1601; 1960), as applied to claims 57, 58, 63, 74-76, 78 and 86-89 above, and further in view of Bova *et al*. (International Publication No. WO99/06046; Cited by Applicant) and Mathias (U.S. Patent No. 7,153,870B2).

The teachings of Carlson *et al*., Gębicki *et al*. and Oettgen *et al*. have been set forth *supra*.

With regard to instant claims 70-72, 77, 79 and 80, Carlson *et al*. fail to disclose specifically wherein the pyridinium derivative is administered together with a cardiovascular agent (instant claim 77). However, Bova *et al*. disclose, in reference claims 33-37, 39 and 40, page 78, a method for altering lipids in an individual without causing drug-induced hepatotoxicity, myopathy or rhabdomyolysis, wherein said method comprising administering to the individual once per day a single dose of a pharmaceutical combination comprising an effective lipid-altering amount of nicotinic acid in an extended release form and an effective lipid-altering amount of an HMG-CoA (3-hydroxy-3-methyl-glutaryl coenzyme A) reductase inhibitor, a cardiovascular agent. In the instant excerpt, Bova *et al*. further disclose wherein the lipids may be triglycerides, and wherein the method reduces triglycerides, increases high-density

lipoprotein (HDL) cholesterol levels, decreases total cholesterol to HDL-cholesterol levels, and decreases low-density lipoprotein (LDL) cholesterol to HDL-cholesterol ratios in the serum of the subject. In the Abstract, Bova *et al*. disclose wherein the present invention also relates to methods of altering serum lipids in subjects to treat hyperlipidemia, which includes hypertriglyceridemia, by administering an oral solid pharmaceutical combination comprising, at least, an HMG-CoA reductase inhibitor and nicotinic acid, a nicotinic acid compound, e.g., nicotinamide (See reference page 15, second paragraph), or mixtures thereof. Additionally, Bova *et al*. disclose, on page 21, last paragraph, wherein the reference invention may be formulated into sustained release granules, beads or pellets, tablets, capsules and sachets, for example, as required by instant claims 70, 79 and 80.

Carlson *et al*. fail to disclose specifically wherein the pyridinium salt of formula I is administered parenterally, or to the airways by inhalation (instant claims 71 and 72, respectively). However, Mathias discloses, in column 15, line 5, through column 17, line 50, nicotinamide derivatives formulated for oral administration, e.g., tablets, capsules and liquids; parenteral administration, e.g., intravenous and intraperitoneal; and inhaled/intranasal administration.

Therefore, a skilled artisan would have envisaged the instantly claimed method of treating hypertriglyceridemia, administering a quaternary pyridinium salt of formula I in combination with a cardiovascular agent, e.g., HMG-CoA, as disclosed by Bova *et al*., through customary routes, e.g., oral, parenteral and inhalation, known to one of ordinary skill, as disclosed by Mathias. One of ordinary skill in the art would have been

motivated to combine the teachings of the aforementioned references when seeking a combination therapy for the treatment of hypertriglyceridemia, wherein customary routes of administration are available to increase the likelihood of patient compliance. It would have been obvious to one of ordinary skill in the art, at the time of the invention, because the combined teachings of the prior art are fairly suggestive of the claimed invention.

Accordingly, the instant invention, as claimed in claims 70-72, 77, 79 and 80, is *prima facie* obvious over the combination of the aforementioned teachings.

Applicant's Arguments

Applicant alleges that though Bova *et al*. teach combinations of nicotinamide with other cardiovascular agents, Bova *et al*. do not detract from the nonobviousness of claims 70-72, 77, 79 and 80, even when considered in combination, since all these claims are dependent on claim 57, and required the use of 1-methylated pyridinium salt of formula I, the nonobviousness of which was discussed above.

Additionally, Applicant alleges that though Mathias does disclose different modes of administration of nicotinamide derivatives that are not related in any manner with quaternary salts of the present formula I, Mathais does not detract from the nonobviousness of claims 70-72, 77, 79 and 80, even when considered in combination, since all these claims are dependent on claim 57, and required the use of 1-methylated pyridinium salt of Formula I, the nonobviousness of which was discussed above.

Examiner's Response

Applicant's Arguments, filed 05/21/2009, have been fully considered but they are not persuasive.

As mentioned *supra*, Bova *et al*. disclose a method for altering lipids, e.g., triglycerides, comprising administering a combination comprising an effective lipid-altering amount of nicotinic acid, or nicotinamide (See page 15, line 9), and an effective lipid-altering amount of an HMG-CoA reductase inhibitor, a cardiovascular agent. Additionally, the Mathias reference was provided to exemplify methods of administration that would have been well within the purview of one of ordinary skill in the art, at the time of the invention. Taken together with the discussion of Carlson *et al*., Gębicki *et al*. and Oettgen *et al*. set forth *supra*, it would have been obvious to one of ordinary skill in the art, at the time of the invention, because the combined teachings of the prior art are fairly suggestive of the claimed invention.

The rejection is **maintained**.

Response to Arguments

The rejection of claims 57, 58, 63, 75-79 and 86-89, provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-15, 19, 22-25, 37, 53 and 54 of copending Application No. 11/484,892 (hereinafter referred to as Application No. '892), is hereby **withdrawn**. The instant claims of Application No. '892 have been amended, and are no longer commensurate in scope with the instant claims.

Double Patenting

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 57, 58, 63, 70, 75, 78, 80 and 86-89 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 6 and 8 of copending Application No. 11/874,627 (hereinafter referred to as Application No. '627).

Although the conflicting claims are not identical, they are not patentably distinct from each other because Application No. '627, in reference claims 1, 5, 6 and 8, is drawn to a method of treating, orally, a lipoprotein abnormality, e.g., hyperlipidemias, which includes hypertriglyceridemia, in a subject in need thereof by administering to the subject a food extract containing N-methylnicotinamide. It is noted that the instant application claims 1-methylnicotinamide, for example. MPEP § 2144.09 (II) states, "Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH_2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

In positional isomerism, a functional group changes position on the chain or ring. As claimed, the positional isomers have substantially similar intended uses as well. As stated *In re Norris* 179 F.2d 970, 84 USPQ 458 (CCPA 1970), a novel useful compound

that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. In other words, if the positional isomers of the instant application produced unexpected results that would not be obvious to one of ordinary skill in the art, said isomers would be patentably distinct; however, there is no evidence of such results in the instant application. Thus, the instant claims are *prima facie* obvious over the prior art.

Accordingly, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's Arguments

Applicant alleges the two applications are not commonly assigned. Applicant respectfully request that the rejection be held in abeyance until the claims are otherwise allowable.

Examiner's Response

According to USPTO records, there is an assignment that is shared. Additionally, it is noted that Jerzy Gębicki is a common inventor. The rejection is **maintained**.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NELSON C. BLAKELY III whose telephone number is (571) 270-3290. The examiner can normally be reached on Mon - Thurs, 7:00 am - 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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August 16, 2009

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